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Certificate of Mailing: Date of Deposit: September 24, 2002

I hereby certify under 37 C.F.R. § 1.8(a) that this correspondence is being deposited with the United States Postal Service as **first class mail** with sufficient postage on the date indicated above and is addressed to the U.S. Patent and Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202.

Elaine Fabrizio

Printed name of person mailing correspondence

Elaine Fabrizio

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Zhu et al.

Art Unit: 1636

Serial No.: 09/613,486

Examiner: K. Katcheves

Filed: July 11, 2000

Customer No.: 21559

Title: GRAPEVINE LEAFROLL VIRUS (TYPE 2) PROTEINS AND THEIR USES

U.S. Patent and Trademark Office
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REPLY TO NOTICE TO COMPLY WITH REQUIREMENTS
FOR PATENT APPLICATIONS CONTAINING
NUCLEOTIDE AND/OR AMINO ACID SEQUENCES

In reply to the Notice to Comply with Sequence Requirements (copy enclosed) included with the Office Action mailed on March 26, 2002, Applicants submit the following:

- ☒ An initial paper copy of the sequence listing and an amendment directing its entry into the specification.
- ☒ An initial copy of the sequence listing in computer readable form.
- ☒ A statement that the contents of the paper and computer readable copies are the

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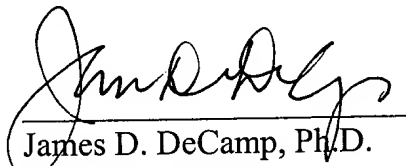
same and contain no new matter.

Enclosed is a courtesy copy of the petition to extend the period for replying for three months, to and including September 26, 2002 that was filed with the concurrently filed Reply to the Office Action dated March 26, 2002.

If there are any other charges, please apply them to Deposit Account No. 03-2095.

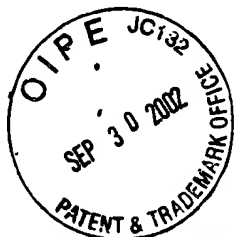
Respectfully submitted,

Date: September 24, 2002


James D. DeCamp, Ph.D.
Reg. No. 43,580

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101 Federal Street
Boston, MA 02110
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07678.062004 Reply to Notice to Comply to Sequence Requirement.doc





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STATEMENT UNDER 37 C.F.R. §§ 1.821 - 1.825

In reply to the Notice to Comply with Sequence Requirements included with the Office Action mailed on March 26, 2002, enclosed is a Sequence Listing in accordance with the requirements of 37 C.F.R. §§ 1.821 through 1.825 and consisting of 37 pages. As is noted in the accompanying Amendment, this Sequence Listing is to be inserted at the end of the application.

As required by 37 C.F.R. § 1.821(c), each sequence in the application appears separately in the sequence listing and each sequence in the sequence listing is assigned a separate sequence identifier.

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As required by 37 C.F.R. § 1.821(d), the sequence identifiers are used throughout the application description and claims to refer to their respective sequences.

As required by 37 C.F.R. § 1.821(e), enclosed is a diskette containing a copy of the sequence listing in computer readable form.

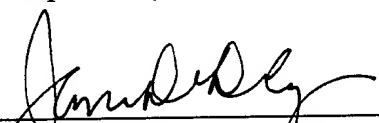
As required by 37 C.F.R. § 1.821(f), I hereby state that the contents of the computer readable form are the same as the contents of the paper copy.

As required by 37 C.F.R. § 1.821(g), I hereby state that this submission contains no new matter.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: September 24, 2002


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Version of Replacement Paragraphs Showing Changes Made,

Pursuant to 37 C.F.R. § 1.121(b)(1)(iii)

Amend the paragraph beginning on page 9, line 18, as follows.

Figure 3A-3D are comparisons between ORF1a/ORF1b of GLRaV-2 and BYV. Figure 3A-3D show the conserved domains of two papain-like proteases (P-PRO), methyltransferase (MT/MTR), helicase (HEL), and RNA-dependent RNA polymerase (RdRP), respectively (SEQ ID NOS: 3, 5, and 24-27). Exclamation marks indicate the predicted catalytic residues of the leader papain-like protease; slashes indicate the predicted cleavage sites. The conserved motifs of the MT, HEL, and RdRP domains are highlighted with overlines marked with respective letters. The alignment is constructed using the MegAlign program in DNASTAR.

Amend the paragraph beginning at page 9, line 25, as follows.

Figures 4A and 4B are alignments of the nucleotide (Figure 4A) and deduced amino acid (Figure 4B) sequences of ORF1a/ORF1b overlapping region of GLRaV-2, BYV, BYSV, and CTV (SEQ ID NOS: 28-35). Identical nucleotides and amino acids are shown in consensus. GLRaV-2 putative + 1 frameshift site (TAGC) and its corresponding sites of BYV (TAGC) and BYSV (TAGC) and CTV (CGGC) at nucleotide and amino acid sequences are highlighted with underlines.

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Amend the paragraph beginning at page 9, line 31, as follows.

Figure 5 is an alignment of the amino acid sequence of HSP70 protein of GLRaV-2 and BYV (SEQ ID NOS: 9 and 36). The conserved motifs (A to H) are indicated with overlines and marked with respective letters. The alignment was conducted with the MegAlign program of DNASTAR.

Amend the paragraph beginning at page 10, line 3, as follows.

Figure 6A is a comparison of the coat protein (CP) and coat protein duplicate (CPd) of GLRaV-2 with other closteroviruses (SEQ ID NOS: 13, 15, and 37-42). The amino acid sequence of the GLRaV-2 CP and CPd are aligned with the CP and CPd of BYV, BYSV, and CTV. The conserved amino acid residues are in bold and the consensus sequences are indicated. Sequence alignment and phylogenetic tree were constructed by Clustal Method in the MegAlign Program of DNASTAR. Figure 6B is a tentative phylogenetic tree of the CP and CPd of GLRaV-2 with BYV, BYSV, CTV, LIYV, LChV, and GLRaV-3. To facilitate the alignment, only the C-terminal 250 amino acids of CP and CPd of LIYV, LChV, and GLRaV-3 were used. The scale beneath the phylogenetic tree represents the distance between sequences. Units indicate the number of substitution events.

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Amend the paragraph beginning at page 10, line 20, as follows.

Figure 9 is an alignment of the amino acid sequence of HSP90 protein of GLRaV-2 with respect to other closteroviruses, BYS, BYSV, and CTV (SEQ ID NOS: 11 and 43-45). The most conserved motifs (I to II) are indicated with the highlighted lines and marked with respective letters.

Amend the paragraph beginning at page 10, line 23, as follows.

Figure 10 is an alignment of the nucleotide sequence of 3'-terminal untranslated region of GLRaV-2 with respect to the closteroviruses BYV (Agranovsky et al., "Beet Yellows Closterovirus: Complete Genome Structure and Identification of a Papain-like Thiol Protease," Virology 198:311-24 (1994), which is hereby incorporated by reference), BYSV (Karasev et al., Organization of the 3'-Terminal Half of Beet Yellow Stunt Virus Genome and Implications for the Evolution of Closteroviruses," Virology 221:199-207 (1996), which is hereby incorporated by reference), and CTV (Karasev et al., "Complete Sequence of the Citrus Tristeza Virus RNA Genome," Virology 208:511-20 (1995), which is hereby incorporated by reference) (SEQ ID NOS: 1 and 46-48). The consensus sequences are shown, and the distance to the 3'-end is indicated. A complementary region capable of forming a "hair-pin" structure is underlined.

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U.S. Serial No. 09/613,486

Clean Version of the Replacement Paragraphs.

Pursuant to 37 C.F.R. § 1.121 (b)(1)(ii)

Figure 3A-3D are comparisons between ORF1a/ORF1b of GLRaV-2 and BYV. Figure 3A-3D show the conserved domains of two papain-like proteases (P-PRO), methyltransferase (MT/MTR), helicase (HEL), and RNA-dependent RNA polymerase (RdRP), respectively (SEQ ID NOS: 3, 5, and 24-27). Exclamation marks indicate the predicted catalytic residues of the leader papain-like protease; slashes indicate the predicted cleavage sites. The conserved motifs of the MT, HEL, and RdRP domains are highlighted with overlines marked with respective letters. The alignment is constructed using the MegAlign program in DNASTAR.

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Figure 5 is an alignment of the amino acid sequence of HSP70 protein of GLRaV-2 and BYV (SEQ ID NOS: 9 and 36). The conserved motifs (A to H) are indicated with overlines and marked with respective letters. The alignment was conducted with the MegAlign program of DNASTAR.

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